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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/337,675	06/22/1999	RAJEEV A. JAIN	029318/0497	9275

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EXAMINER	
TRAN, SUSAN T	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/337,675	JAIN ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 25-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 25-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/06/07 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 41, 45 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims contain the trademark/trade name "Tetronic 1508®" and "Crodesters® SL-40". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods

themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the surface stabilizer and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

Claims 1, 2, 8-22, 25-31 and 34-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desieno et al. US 5,573,783, in view of Liversidge et al. US 5,145,684 and Mody et al. US 5,853,756.

Desieno teaches a pharmaceutical film matrix comprising nanoparticles of a low solubility drug associated with a steric stabilizer (surface stabilizer), and over coated with a protective layer (abstract). Desieno also teaches the drug particles having extremely small effective average particle size can be prepared by wet milling in the presence of grinding media in conjunction with a surface modifier (column 2, lines 51-55). The effective average particle size is less than about 400 nm (column 6, lines 15-24). Suitable drug substances are disclosed in column 3, lines 16-46, which includes naproxen and cyclosporin. The steric stabilizers are disclosed in column 3, lines 56-65, but the most preferred steric stabilizer is polyvinylpyrrolidone (column 4, lines 22-23). The protective layer over coated the film matrix comprises polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) (column 5, lines 1-13). Column 4, lines 42-67 discloses the process for preparing the nanoparticles, wherein water is used for the dissolution

and suspensions steps is also disclosed. Examples 1 and 2 show the amounts of drug that falls within the claimed range.

Desieno does not expressly teach the time period of controlled release from about 2 to about 24 hours.

Mody teaches a controlled release formulation comprising a controlled release coating composed of mixture of polyethylene glycol and polyvinylpyrrolidone (abstract; column 2, lines 48-60; and example 6). Example 6 specifically teaches mixture of polyvinylpyrrolidone and polyethylene glycol provides controlled release of up to 24 hours. Thus, it would have been obvious to one of ordinary skill in the art to prepare a controlled release dosage form from the combination teachings of Desieno and Mody, because Mody teaches mixture of polyvinylpyrrolidone and polyethylene glycol release active drug in a controlled manner for maintaining minimum effective concentration levels over longer duration ranging from 12-24 hours, and because Desieno teaches the desirability of coating drug substances with composition comprising mixture of polyvinylpyrrolidone and polyethylene glycol to obtain formulations useful in pharmaceutical art.

Desieno further does not explicitly teach the particle distribution. However, it is well known in pharmaceutical art that the term "effective average particle" means at least 50% of the particle population. To be more specific, Liversidge teaches a dispersible particle made of a drug substance and a surface modifier adsorbed on the surface of the drug substance to maintain *an effective average particle size* of less than about 400 nm (abstract). The term "effective average particle size" is defined by

Liversidge as at least 90% of the particle have an average particle size of less than 400 nm measured by using the technique that is so well known in pharmaceutical art (column 5, lines 20-39). Thus, one of ordinary skill in the art would have been motivated to, by routine experimentation prepare a nanoparticles formulation for low solubility drugs having effective average particle size that falls within the claimed range, because Desieno teaches nanoparticles having effective average particle size is less than about 400 nm, and because Liversidge teaches nanoparticles with at least 90% of the particle have an average particle size of less than 400 nm to obtain pharmaceutical formulations useful in pharmaceutical art.

Claims 3-7, 32, 33 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desieno et al. US 5,573,783, in view of Liversidge et al. US 5,145,684 and Mody et al. US 5,853,756 and Friend et al. US 5,811,388.

Desieno is relied upon for the reason stated above. Desieno does not expressly teach the concentration of the rate-controlling polymer, the binder, and the lubricant.

Friend teaches a tablet dosage form made of matrix composed of drug dispersed in hydrocolloid and excipients (abstract, and column 5, lines 49-53). The excipients, such as binders, diluents, and lubricants are present at a level of from about 2-50% (column 11, lines 22-65). The excipients further include HPMC, PVP, and cellulosic derivatives (column 12, lines 1-33). Suitable lubricant, such as magnesium stearate are mixed with the drug substance and HPMC and then compressed into tablet (column 17, lines 56-61). The tablet is further coated using enteric coating polymers selected from

cellulose acetate phthalate, polyvinyl acetate phthalate, methacrylic acid, and those polymers having the trade name Eudragit in an amount of from about 0.5 to about 10% (column 14, lines 20-62). Thus, it would have been obvious for one of ordinary skill in the art to modify the nanoparticle of Desieno and Liversidge using the excipients and the enteric coating polymers in an effective amount in view of the teachings of Friend, because Friend teaches a tablet dosage form suitable for controlled release of poorly soluble drug substance. The expected result would a controlled release film matrix coated carrier that exhibits excellent bioavailability and extremely stable.

Response to Arguments

Applicant's arguments filed 07/06/07 have been fully considered but they are not persuasive.

Applicant argues that it is well known in the art that the presence of polyethylene glycols having low average molecular weight, such as an average molecular weight in the range of 300 to 8,000, in drug formulations causes a fast drug dissolution rate, because the polymer is in a fluid state and maintains the fluidity of the drug composition when water is imbibed into the drug matrix. High molecular weight polyethylene glycols, high molecular weight PVP, high molecular weight plant exudates or enteric polymers, such as those used in the present application, on the other hand, after imbibing water tend to be viscous and less fluid, thus slowing the drug dissolution rate and providing drug controlled release.

In response to applicant's argument that "it is well known in the art that the presence of polyethylene glycols having low average molecular weight, such as an average molecular weight in the range of 300 to 8,000, in drug formulations causes a fast drug dissolution rate, because the polymer is in a fluid state and maintains the fluidity of the drug composition when water is imbibed into the drug matrix", it is noted that the art teaches the present of PEG with molecular weight as low as 400 provide sustained/controlled release of active substance (see for example Mughal et al. US 4,524,060 at column 3, lines 6-25). In view of the above cited Mody et al., as well as the teaching of Mughal (cited herein solely as a teaching reference), it is concluded that there is evident in the prior arts that the present of low molecular weight PEG does not necessarily result in a fast drug dissolution rate, but rather a controlled/sustained release profile.

Applicant argues that in contrast to the present invention, Desieno discloses PVP/PEG polymers having an average molecular weight of 7,000 at the most, and describes polyethylene glycols having average molecular weights in the range of 300 to 8,000, with polyethylene glycol 3350 being the preferred PEG of the invention. *See* col. 5, lines 22-25. The Povidone (k15/17) used in Example 3 of Desieno, for example, has an average molecular weight of 10,000 (see Exhibit A).

However, the present specification does not provide any guidance as well as definition for the limitation "high molecular weight" recited in the present claims. As such, the examiner relied upon the well known facts taught in the art which teaches high molecular weight, in deed, *very* high molecular weight starts from about 10,000 (see for

example Harkness et al. at column 4, line 51; and Fitzgerald et al. at column 2, lines 58-60). Thus, Desieno suggests the use of PVP having molecular weight that falls within the range of high molecular weight.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER
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